

## Cartilage Volume Quantification via Live Wire Segmentation<sup>1</sup>

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**Rationale and Objectives.** A reduction in cartilage volume is characteristic of osteoarthritis and hence there exists a need for an accurate and reproducible method to measure in vivo cartilage volume. Quantification of cartilage volume from magnetic resonance (MR) images requires a segmentation technique such as the user-driven “Live Wire” strategy that can reliably delineate object volumes in a time-efficient manner. In the present work, the accuracy and reproducibility of the Live Wire method for the quantification of cartilage volume in MR images is evaluated.

**Materials and Methods.** The accuracy of the Live Wire method was assessed by comparing the MR-based volume measurement of a patellar cartilage-shaped phantom versus data calculated via water displacement. The inter- and intra-operator reproducibility of the technique was evaluated from Live Wire segmentation of the patellar cartilage volume from fat-suppressed 3-dimensional spoiled-gradient-echo images of five healthy human volunteers performed by three operators. To provide data for analysis of inter-scan reproducibility, the human scans were repeated five times with the aid of a leg-restraining jig to minimize repositioning error.

**Results.** The volume of the patellar cartilage-shaped phantom measured via Live Wire segmentation of MR images was within 97.8% of its true volume. The average inter- and intra-operator coefficients of variation of three operators were 3.0% and 0.4%, respectively. The average inter-scan coefficient of variation of five repeated scans of each volunteer was 2.7%.

**Conclusion.** The data suggest that the Live Wire strategy is an accurate, reproducible, and efficient technique to measure cartilage volume in vivo in a feasible amount of operator time.

**Key Words.** Cartilage; volume; segmentation; Live Wire.

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Osteoarthritis (OA) is a chondro-degenerative joint disease characterized by pain, swelling, stiffness, and ultimately joint immobilization. The hallmarks of OA are severe cartilage clefting, thinning, and volume reduction.

At present, the diagnosis and monitoring of OA hinges largely around the use of traditional radiography to detect these late-stage events that are commonly manifested as joint-space narrowing between radio-opaque bony structures (1,2). Despite its conventionality, joint-space measurement has appreciable limitations as both a diagnostic and evaluative technique. Comparison of measurements of joint-space narrowing are prone to errors in patient positioning (3) and subjective image interpretation (4). In addition, the limited sensitivity of the technique requires substantial loss of cartilage volume before it can be detected as joint-space narrowing (5).

Magnetic resonance imaging (MRI) has been established as the method of choice to directly visualize carti-

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lage noninvasively. The 3-dimensional (3D) coverage of an entire cartilaginous region by MRI allows for the direct quantification of cartilage volume. Several groups have developed sophisticated techniques to quantitatively measure cartilage volume, thickness, and surface area based on MRI data (6–13). Measurements of cartilage volume via MRI have been previously shown to correlate well with qualitative evaluation of pain, stiffness, and physical dysfunction assessed via the WOMAC test (14). The measurement of cartilage volume also provides quantitative data with which to monitor the progression of OA (13). Such data could be beneficial not only in the longitudinal monitoring of the OA, but also in the evaluation of potential therapeutic agents.

An important aspect of many cartilage volume quantification methods is the accurate segmentation of cartilage from surrounding tissue. The ideal segmentation strategy is one that produces accurate and precise results in a reasonable amount of time with minimal subjectivity. The least sophisticated method is manual segmentation whereby an operator on a computer workstation freely draws a boundary on an image to indicate the location of an object (7,15). The process of manually locating the boundary, while straightforward, can be time-consuming and subject to operator bias and error. Automated methods, such as those based on edge-detection (8), can quickly segment the cartilage with little or no user interaction by using signal intensity information. An example of a partially automated method is a region-growing algorithm that determines cartilage volume based on neighborhood connectivity starting with an operator-placed seed pixel (11,16,17). However, automated methods can be sensitive to image contrast and signal-to-noise ratio (SNR) which can potentially result in grossly inaccurate positioning of the cartilage boundary. User-driven segmentation methods combine the sensibility of a human operator in the recognition of the object boundary with the reliability of a computer to quickly and reproducibly delineate the boundary. In an implementation of a user-driven segmentation strategy, an operator guides the recognition of the boundary and the computer performs the delineation based on information gathered from image data. Examples of such methods include deformable contours using B-spline snakes (10,18), active contours (6), and active shape models (9).

A promising user-driven segmentation strategy is the "Live Wire" algorithm (19). In the initial step of the Live Wire method, an operator trains the algorithm by using a reference image set. The algorithm automatically creates mathematical functions with which to delineate boundaries between cartilage and other tissue. The training process gen-

erally takes less than 5 minutes and needs to be performed only once. After training, an operator can segment cartilage from any similar image set by manually guiding the cursor near the cartilage boundary. Based on its training, the Live Wire algorithm assists the operator by automatically positioning the border at the ideal location between cartilage and other tissue. In this manner, the operator can quickly and accurately segment the cartilage in a total time of approximately 30 seconds per slice. One strength of this technique is that no post hoc correction is required because it exploits the synergy that exists between superior human recognition and superior computer delineation.

The purpose of this work is to evaluate the ability of the Live Wire technique to measure cartilage volume from MR images. Accuracy of the method is determined by comparing the MRI-based quantification of the volume of a patellar cartilage-shaped phantom with the gold standard estimation by the method of water displacement. The reproducibility of in vivo volume quantification is assessed by measuring inter- and intra-operator and inter-scan coefficients of variation of the measurement of the volume of patellar cartilage of healthy human volunteers.

## MATERIALS AND METHODS

### Human Subjects

The University of Pennsylvania's Institutional Review Board granted approval for all studies involving human subjects undertaken in this work. Five healthy male volunteers (ages 21–29 years; mean, 23 years) were selected based on inclusion criteria such as no history of joint pain as determined by a physician. Women of child-bearing age, children, and older adults possibly with thin or damaged patellar cartilage were excluded.

### Assessment of Accuracy

The accuracy of Live Wire was assessed by comparing the volume of a patellar cartilage-shaped phantom as calculated by segmentation of MR images with the gold standard volume estimated via water displacement. The patellar cartilage-shaped phantom was constructed by using the following methods. The complete patellar cartilage was removed in one portion from a bovine patella using a scalpel and a Dremel power tool (Dremel, Racine, WI). Bone fragments were removed from the bone/cartilage interface and the patella was soaked for 2 hours in phosphate-buffered saline. The cartilage was then suspended in approximately 300 mL of Smooth-Sil 910 silicone molding compound (Smooth-On,

Inc, Easton, PA) contained in a plastic cup. Following a 24-hour hardening period, the mold was removed from the cup and the cartilage was extracted from the top of the mold through an incision. After rinsing and drying the outer surface and inner cavity, the dry weight of the mold was recorded. The mold was then submerged in distilled water until the entire inner cavity was filled. Air bubbles were removed from the inner cavity by running a cotton swab along the entire cavity surface while the mold was held submerged. Excess water was blotted from the outside of the mold before weighing. The self-sealing properties of silicone ensured no water leakage from the mold during this process. The volume of the patellar cartilage-shaped space was calculated by measuring the difference in weight between the empty mold and the water-filled mold. This process was repeated five times and volumes from all trials were averaged. Before imaging, the filling process was repeated with 10 mmol/L CoCl<sub>2</sub> solution to reduce the T<sub>1</sub> relaxation time of water to enhance SNR in the image data.

Much attention has been given to the fat-suppressed spoiled gradient-echo (SPGR) pulse sequence and variants thereof as a means to produce MR images in which cartilage can be accurately distinguished from surrounding tissue (15,17,20). This sequence is commonly used to produce images with excellent cartilage-to-bone contrast in reasonable scan times. We also chose to use the SPGR sequence to image both the phantom and human subjects. All imaging was performed on a 4 Tesla Signa whole-body scanner (General Electric Medical Systems, Waukesha, WI) at the Hospital of the University of Pennsylvania (Philadelphia, PA). The imaging of the phantom was carried out using a 3D fat-suppressed SPGR sequence using a 3-inch diameter surface coil encompassing the phantom with the following parameters: FOV = 8 cm × 8 cm × 4.2 cm, TE/TR = 20/60 ms, flip angle = 45°, and a 512 × 512 × 28 acquisition matrix.

To ascertain the effect of image quality on segmentation precision, the SNR and phantom boundary in the original images were artificially degraded to varying degrees by using computer simulations performed in IDL (RSI, Boulder, CO). The SNR of the original data set (40:1) was reduced by adding zero-mean Gaussian distributed noise with varying amplitude to achieve SNR values of 5:1, 10:1, 20:1, and 30:1. The phantom boundary in the original data set was blurred by convolving each image with a 2-dimensional Gaussian kernel of varying widths of 0 (no blurring), 5, 9, and 13 pixels. Combinations of the five SNR-degraded data sets with the four blurring kernels generated a total of 20 data sets. The phantom boundary was segmented from the data sets by a

single operator (A.J.G.) using the Live Wire tool implemented within the 3DVIEWS software system (Medical Image Processing Group, Department of Radiology, University of Pennsylvania, freely available at [www.mipg.upenn.edu](http://www.mipg.upenn.edu)). A shape-based interpolation technique (21) was applied to the segmented data to generate a 3D isotropically sampled binary volume. The volume of the cartilage was estimated from the total voxel count within the interpolated 3D binary volume. The MRI-based volumetric measurements were compared with the gold standard data estimated from water displacement.

### Assessment of Precision

MR image sets of the right knee joints of five volunteers were collected using an 8-inch diameter surface coil placed on top of the knee. A larger surface coil was used to collect the phantom data to capture the entire patella. Image data sets were collected in the axial plane covering the patella using a 3D fat-suppressed SPGR sequence with the following parameters: FOV = 8 cm × 8 cm × 4.2 cm, TE/TR = 20/60 ms, flip angle = 60°, and a 512 × 256 × 28 matrix to collect each image set in approximately 8 minutes. To assess the inter-scan reproducibility of the Live Wire-based volume estimation, the scans were repeated five times for each volunteer. In between each of the five scans, volunteers were asked to leave the scanner table so that each repeat scan was independently acquired. Care was taken in repositioning the volunteer's leg during each repeat scan by using a custom-built jig equipped with foot and thigh retaining straps (Fig 1) so that roughly the same region of the knee was considered within the field of view. With the assistance of position measurements recorded from the rulers affixed to the jig, each volunteer's leg was repositioned within the scanner with some consistency. The measurement of in vivo patellar cartilage volume was performed in a manner similar to that for the phantom data. Three operators segmented the patellar cartilage from each of the five data sets for all five volunteers. The three operators performed the segmentation of each data set two times to provide data for the analysis of intra-operator variability. To assess intra-operator variability, the volume measurements of the two segmentations performed by each operator on every data set were compared. Inter-operator variability was measured as the differences in the average measurement of volume by all three operators. Inter-scan variability was assessed according to the differences in the volume quantification performed by a single operator (A.J.G.) from each of the five scans for every volunteer. Inter-/intra-operator and inter-scan variations were expressed by percent coefficient of variation (%CV) (ie, standard deviation expressed as a percent of the mean).

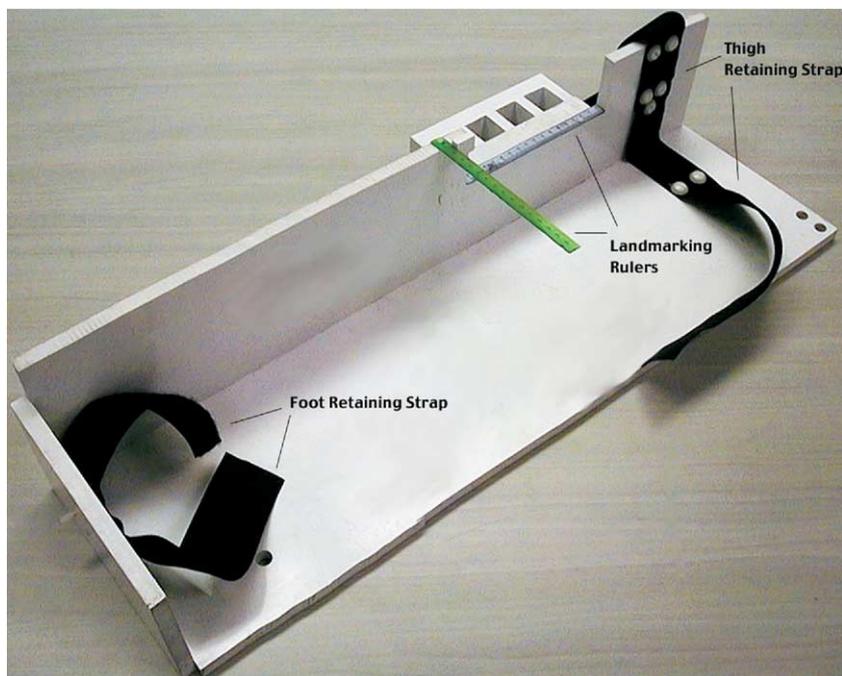


Figure 1. Custom-built PVC leg-restraining jig.

## RESULTS

### Analysis of Live Wire Accuracy

Figure 2 displays volumetric data calculated from the segmentation of the original patellar cartilage-shaped phantom data set and 19 artificially degraded reproductions of this data set. The gold standard water displacement measurement of the phantom volume ( $10.2 \pm 0.15 \text{ mm}^3$ ) is also plotted as the first bar in each series as a reference. For reasonable values of SNR ( $\geq 10:1$ ) and blurring ( $\leq 9$  pixels), the Live Wire strategy was able to accurately measure the volume of an irregularly shaped human-sized object with clinically feasible imaging pa-

rameters and pixel resolution as evidenced by the low errors displayed in Fig 2. Segmentation of the original phantom data set (SNR = 40:1, no additional blurring) yielded an error of 2.2% compared with the gold standard volume estimated via water displacement.

### Analysis of Live Wire Precision

A typical slice from the middle of a representative in vivo data set is shown in Fig 3A. Figure 3B shows two segmentations of this slice performed by two different operators. The segmentation of each data set of 28 slices was generally accomplished in an average of less than 15 minutes per operator. The two segmenta-

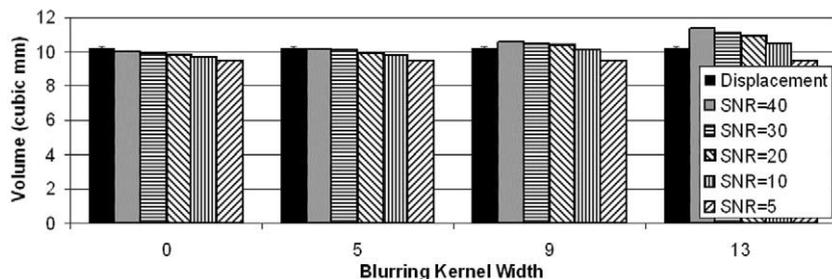
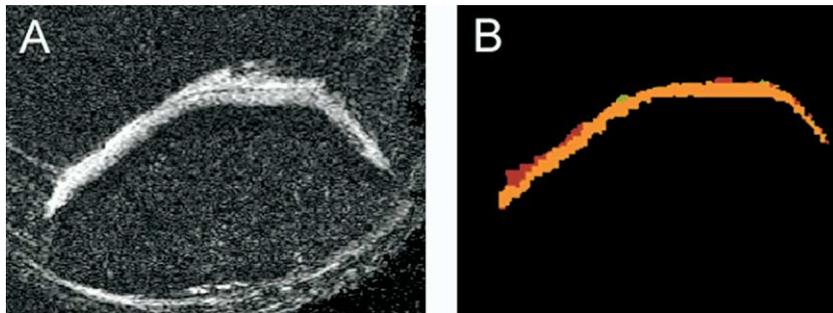


Figure 2. Volumes of the original patellar cartilage-shaped phantom and 19 additional artificially degraded data sets. Phantom volume as measured by water displacement is plotted as the first bar in each series as a reference.



**Figure 3.** A typical middle slice from an in vivo data set of the human knee (A). Two Live Wire segmentations of this slice, one by each of two operators (B). The overlapping areas of mismatching segmentation are displayed in white.

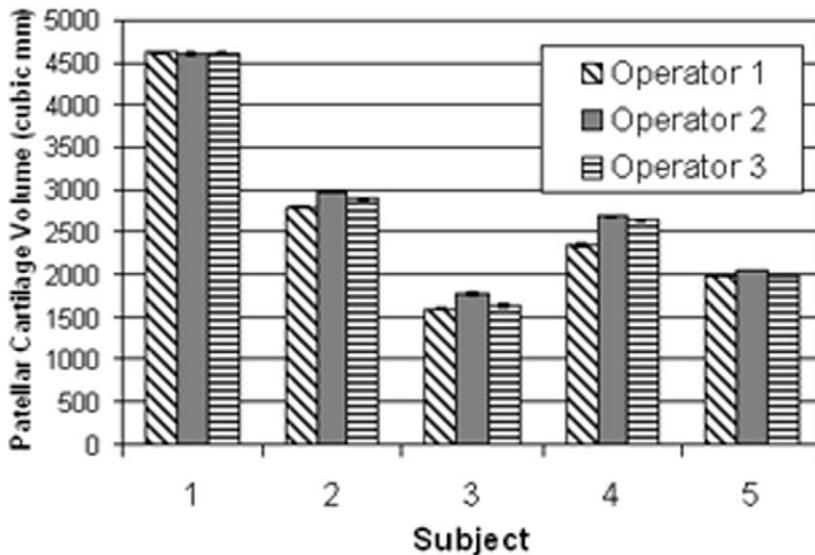
tions differ most dramatically toward the lateral periphery of the patella corresponding to the region of weakest contrast between cartilage and the surrounding tissue/fluid. Contrarily, the two segmentations showed the greatest agreement along the cartilage/bone interface, the region of sharpest contrast. This trend, observed in all in vivo data sets gathered for this study, illustrates how segmentation reproducibility is compromised by the lack of contrast.

The mean patellar cartilage volumes for the five human subjects ranged from 1,667.8 mm<sup>3</sup> to 4,611.8 mm<sup>3</sup> (Fig 4). Two independent segmentations by three operators on all five subjects yielded an average intra-operator %CV of 0.4 ± 0.3 (mean ± standard deviation). The low

intra-operator %CV is evidence of the consistency of the Live Wire technique in placing the borders in nearly the same positions time after time. An average of the mean volumes generated by the three operators yielded an average inter-operator %CV of 3.0 ± 2.6. Inter-scan %CV as determined by the segmentation of five data sets gathered on each of the subjects ranged from 1.5 to 3.8. The average inter-scan %CV was 2.7 ± 1.0.

**DISCUSSION**

The Live Wire method produced measurements of accuracy, intra- and inter-operator and inter-scan %CV that



**Figure 4.** Patellar cartilage volume of five subjects as determined from two segmentations by each of three operators.

**Table 1**  
**Summary of the Measurements of Cartilage Volume Error, Intra- and Inter-operator and Inter-scan Coefficient of Variation (%CV) for the Live Wire Technique in this Study**

	Live Wire	Manual (5)	Edge Detection (6)	Region-growing (9)	B-spline	Active Contour (4)
Volume Error (%)	2.2*	8.3	-	3.3 (20) <sup>†</sup>	-	<0.5*
Intra-operator % CV	0.4	3.0	3.6	1.6	-	-
Inter-operator % CV	3.0	8.8 (16)	4.4	1.8	4.9 (16)	-
Inter-scan % CV	2.7	-	3.8	1.3	3.9 (8)	<0.2

NOTE: Listed for comparison are sample data from other segmentation techniques gathered from the literature. All data in our study are collected from in vivo images of the patella unless otherwise noted.

\*Data collected using an anatomically shaped phantom.

<sup>†</sup>Compared with measurements obtained via computed tomography

are similar to those reported by studies using other segmentation strategies. Table 1 provides a reference summarizing the error and variability data from several representative reports. The referenced data were obtained using experimental designs similar to that used in this study, namely with regard to the image acquisition protocol. In general, the performance of any segmentation strategy will be affected by image orientation, resolution, and SNR. Although the comparison data were acquired with similar imaging protocols, small variations in the choice of experimental parameters may confound direct comparison between segmentation methods.

A portion of the discrepancy between the MRI-based volume measurements and water displacement data in this work can be attributed to sources that degrade image resolution. Contributions from diffusion, susceptibility, and partial volume effects are known to produce a blurring in MR images, which can obscure the border of objects resulting in inaccurate volumetric data (22). As the extent of these blurring effects is increased, as simulated in this work by blurring with a Gaussian filter, the error in volume increases because of incorrect positioning of the object boundary. Analysis of the data set blurred with a 13-pixel width Gaussian kernel (most blurred) yielded an 11.9% increase in segmented volume compared with the original image. Also, as the SNR of the image sets was decreased, the contrast between the object and its surroundings was degraded resulting in increased error.

The low inter-operator %CV indicates that the Live Wire technique is generally operator-insensitive. However, such user-driven strategies are not as operator-insensitive as a more automated method such as region-growing segmentation. The assistance of the mathematical functions in placing the segmentation boundary aids the operator in locating the boundary position, thereby greatly

reducing operator-dependent variations. The Live Wire algorithm itself does most of the work in boundary location, with the operator acting more as a guide than an instructor. It is important to note that a poorly trained session of Live Wire may not produce such a low intra- and inter-operator %CV. As with any other user-driven segmentation strategy, the training and experience of the individual operators themselves will influence the reliability of the technique. The three operators in this report were not equally experienced and this discrepancy is reflected in part in the measurement of %CV.

The use of the leg-restraining jig greatly aided the process of repositioning of each subject's leg during the repetition of the scans. With the help of the jig, we were able to place the subject's knee in nearly the same position and orientation within the scanner each time. Other reports have indicated that using such a jig can contribute to lowering the inter-scan %CV of quantitative MR measurements (23). Such a device could help ensure consistent positioning of the knee if incorporated into an experimental protocol for longitudinal studies of cartilage volume measured via MRI.

The thickness and regular shape of the patella cartilage made it an easily identifiable object for analysis of cartilage volume. The patellar cartilage lacks adjacent structures such as menisci which may confound object segmentation. Measurement of the more irregularly shaped and thinner tibial or femoral cartilage volume may not produce the same results observed in this study. Therefore, the data presented here can be considered a best-case scenario. Furthermore, the image data in this study were collected on a 4T MR scanner which is not prevalent in clinical use. The greater SNR gained by operating at the higher field strength contributes positively to minimizing error and CV% as observed in analysis of the SNR-degraded phantom data. Were the data collected on more commonly encountered scanner (1.5 or

3T), the observed error and CV% data may not be as low as those reported in this study. In addition, it is important to note that the image processing time needed to complete a Live Wire segmentation is on the order of minutes, much longer in comparison to many automated methods which take only seconds. In our study, we found that it took an experienced user approximately 15 minutes to segment a data set of 28 slices. However, for a specific application this duration could be more or less depending on the quality of the image data, the object to be segmented, and experience of the user. The total time to process a full set of images can possibly encroach on allowable limits if the number of image slices is large.

## CONCLUSION

In this work, the Live Wire method was shown to produce accurate and reproducible measurements of patellar cartilage volume under clinically feasible experimental conditions and image resolutions. The Live Wire strategy provides a quick, accurate, and consistent method to measure volume from in vivo image sets with minimal operator sensitivity. Such techniques can be potentially useful for the measurement of changes in cartilage volume in longitudinal studies of chondro-degenerative diseases.

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